REMARKS

Status of the Claims

Claims 1, 2, 4, 6, 7 and 10 are currently pending in the application. Claims 1-13 stand rejected. Claims 1, 4, 6, 7 and 10 have been amended. Claims 3, 5, 8, 9 and 11-13 have been cancelled. All amendments and cancellations are made without prejudice or disclaimer. No new matter has been added by way of the present amendments. Specifically, the amendment to claim 1 is supported by cancelled claims 3 and 5. Other claim amendments were made to update dependencies of dependent claims and to remove redundant claims as a result of the amendment of claim 1. Reconsideration is respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-3, 4, 7, 10 and 13 stand rejected under 35 U.S.C. § 102(b) as being anticipated by De Giorgio et al., U.S. Patent No. 5,804,402 (hereinafter referred to as "De Giorgio et al."). (*See*, Office Action of July 1, 2008, at pages 2-3, hereinafter, "Office Action"). Claims 3 and 13 have been cancelled herein without prejudice or disclaimer, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

The Examiner states that De Giorgio et al. disclose a reagent for the determination of an analyte concentration in a patient, wherein there is no loss in function of the reagent throughout at least 6-8 months of storage of said reagent at 2 °C to 8 °C. The Examiner states that De Giorgio et al. disclose the use of glucose-6-phosphate dehydrogenase and D-glucose as the enzyme-substrate pair and analytes selected from aspartate transaminase, alanine transaminase and blood urea. (*Id.* at page 3).

Although Applicants do not agree that claim 1 is anticipated by De Giorgio et al., to expedite prosecution, claim 1 has been amended to recite the limitations of claims 3 and 5. The Examiner has indicated that claim 5 is not anticipated by De Giorgio et al. Thus, it is believed that claim 1 is novel and recites non-anticipated limitations previously recited in dependent claim 5.

Applicants contend that their invention is patentably distinct from the disclosure of De Giorgio et al. The difference between the presently claimed invention and that disclosed in De Giorgio et al. is not related to using or not using dynamic stabilization technology to afford continuous regeneration of the coenzyme. Rather, De Giorgio et al. emphasize that their patent has "incomplete specificity for each other," at column 7, line 5. De Giorgio et al. also provide at column 7, line 30:

> In a preferred embodiment of the invention, the degree of specificity between the substrate and enzyme of the coenzyme reduction system is preferably less than 100%, more preferably less than 50% and most conveniently less than 10% on an equimolar basis. Optimally, an enzyme/substrate pair having a cross-reactivity of less than 5% on an equimolar basis may be used.

Thus, according to the disclosure of De Giorgio et al., the method of De Giorgio et al. is thought to be impossible if conducted using "complete specificity" or "100% specificity." However, Applicants have found that in fact, under ideal conditions, one can take advantage of a "completely specific enzyme/substrate pair" and achieve complete specificity. This concept is new, as highlighted by the disclosure of De Giorgio et al.

Dependent claims 2, 4, 7, and 10 are not anticipated as, *inter alia*, depending from a non-anticipated base claim, claim 1.

Reconsideration and withdrawal of the anticipation rejection of claims 1, 2, 4, 7 and 10 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-13 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over De Giorgio et al., De Giorgio et al. U.S. Patent No. 5,705,356 (hereinafter, "De Giorgio II") and Cozzette et al., U.S. Patent No. 6,306,594 (hereinafter, "Cozzette et al."). (*See*, Office Action, at pages 3-5). Claims 3, 5, 8, 9 and 11-13 have been cancelled, thereby obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims.

The Examiner states that De Giorgio et al. and De Giorgio II do not disclose or suggest the specific concentrations of enzyme/substrate recited in the dependent claims. The Examiner states that De Giorgio II disclose testing various amounts of enzyme/substrate to determine the proper regeneration levels. (*Id.* at page 4). Further, the Examiner cites to the disclosure of Cozzette et al. for the proposition that one of ordinary skill in the art is familiar with microfabricated biosensors which include bioactive molecules which may be used in analytical determinations. (*Id.*). The Examiner concludes that one of ordinary skill in the art could have combined these teachings to determine the levels of reagent recited through simple experimentation to obtain a regeneration system "so that the sensor is able to perform multiple measurements." (*Id.* at page 5).

However, it is noted that neither De Giorgio et al. nor De Giorgio II disclose or suggest the concentrations of enzyme/substrate recited in the present claims, at least as amended. The Examiner has admitted this fact with respect to the disclosure of De Giorgio et al. (*Id.* at page 2,

claim 5 not indicated as anticipated). On the other hand, De Giorgio II instruct one of ordinary skill in the art to utilize relatively very large concentrations of enzyme/substrate. For instance, at column 10, lines 33-36 instruct that the optimal range is from 2,500 to 5,000 U/L of G-6-P-DH.

In contrast, Applicants claims recite a concentration of G-6-P-DH of 2-100 U/L. Applicants have discovered a reagent system which is much more sensitive than that disclosed in De Giorgio et al. or De Giorgio II and which utilizes 250 to 2,500 fold less enzyme and substrate. One of ordinary skill in the art could not have predicted that the presently claimed reagent system would function under such conditions. Certainly the cited disclosures provide no rationale or indication that use of 250 to 2,500 fold less reagent would be feasible.

Thus, the cited references in fact teach away from the presently claimed invention. A reference which leads one of ordinary skill in the art away from the claimed invention cannot render it unpatentably obvious. (*See*, *Dow Chem. Co. v. American Cyanamid Co.* 816 F2d 617, (CAFC 1987)). In determining the scope and content of the prior art, and determining whether the prior art suggested the claimed invention, the references "must be read as a whole and consideration must be given where the references diverge and teach away from the claimed invention." (*See*, *Akzo N.V. v. United States Int'l Trade Comm'n*, 1 U.S.P.Q.2d 1241, 1246 (Fed. Cir. 1986); *In re Fine*, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988)).

Further, Applicants note that if a concentration of enzyme/substrate that is too high is used in the method of De Giorgio et al., this will result in a rate of regeneration of ß-NADH which is too fast. This will result in a negative intereference in the assay. (*See*, specification, at paragraph 3, page 5). Applicants note that a concentration of glucose dehydrogenase / D-glucose of between 2 and 100 U/L, used for regeneration of ß-NADH from the oxidized form of NAD,

assures that the concentration of ß-NADH is stabilized. (*See*, specification, at page 6, paragraph 3, line 13). The concentrations recited in the present claims were empirically determined by Applicants and disclosed in the present specification.

Moreover, De Giorgio et al. utilize a large range of concentrations of glucose dehydrogenase and D-glucose, which leads to the possibility of introducing other enzymes into the assay. However, with the presently claimed reduced concentrations of these enzymes, such possible contamination of other enzymes is avoided. The reduction in the amount of reagents utilized in the assay also has the beneficial effect of increasing the long-term stability of the reagents in storage.

Thus, one of ordinary skill in the art could not obtain the presently claimed invention without significantly deviating from the disclosure of De Giorgio et al. The lower amounts of reagents utilized in the presently claimed invention also reduces costs and reduces possible contamination and intereference by other enzymes.

Therefore, Applicants believe that none of the remaining pending claims, at least as amended, are obvious in light of the combined disclosures of the cited references.

Reconsideration and withdrawal of the obviousness rejection of claims 1, 2, 4, 6, 7 and 10 are respectfully requested.

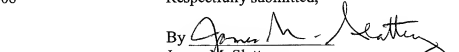
CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: October 1, 2008

Respectfully submitted,

By 

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